REMARKS/ARGUMENTS

Claims 1, 2, 4, 6-9, 11-18, 49-50, 60 and 61 are pending in the instant application. Claims 4 and 11-18 have been withdrawn. Applicants respectfully request rejoinder of these claims. Applicants have canceled claims 10, 51 and 52. Applicants reserve the right to pursue the subject matter of these claims in a continuation application. Applicants have amended claim 1. Support for the amendment to claim 1 can be found, for example, at paragraphs [0014] and [0054] of the instant specification. Applicants have also added new claim 61. Support for claim 61 can be found, for example, at paragraph [0037] of the instant specification. No new matter has been added.

Applicants submitted claim amendments and remarks similar to those presented herein in the April 19, 2011 Response. However, the Examiner indicated that these claim amendments would not be entered. (*See* Advisory Action). Thus, Applicants herein address the rejections set forth in the Final Office Action.

Rejections under 35 U.S.C. § 102

The Examiner has maintained the rejection of claims 1, 2, 6-10, 49-50 and 60 under 35 U.S.C. § 102(a) for being anticipated by Imai *et al.* Ped. Nephrol. 17:790-794 (2002) ("Imai"). Applicants have canceled claim 10, rendering this rejection moot as it regards this claim. The Examiner argued that despite the claims being amended to encompass "isolated mesenchymal stem cells" that Imai still anticipates claims 1, 2, 6-10, 49-50 and 60. The Examiner alleged that the term "isolated" has not been accorded any particular definition in the specification. (*See* Final Office Action at pages 3-5).

Applicants respectfully disagree, but to facilitate prosecution, have amended claim 1, from which claims 2, 6-9, 49-50 and 60 depend. Claim 1 has been amended to be limited to mesenchymal stem cells that are expanded *in vitro* to produce an enriched population of mesenchymal stem cells and to a method of treating acute kidney dysfunction in a subject in need thereof. Imai does not teach this limitation. Further, claim 1 has been amended to be limited to the treatment of acute kidney dysfunction. Imai does not teach this limitation either.

As explained in the April 19, 2011 Declaration under 37 C.F.R. § 1.132 by Robert Brenner (copy enclosed), Imai does not teach the treatment of acute kidney dysfunction nor does it teach a subject in need thereof. Imai teaches an anti-Thy 1 antibody mediated glomerulonephritis (Thy 1 nephritis), a self-limiting disease to explore the involvement of bone marrow derived cells in glomerular remodeling.[1/] Thy 1 nephritis is a model of antibody-mediated glomerular disease.[2/] As the authors recognize, in Thy 1 nephritis normal mesangial cells (mesangial cells are macrophage like cells that are only found within the glomerulus) are disrupted (mesangiolysis), followed by an increase in the number of glomerular cells and subsequent glomerular remodeling.[3/]

Importantly, Thy 1 nephritis is not a model of classic acute kidney injury. Ischemia reperfusion injury is a completely different model of kidney injury. Renal artery clamping results in initial ischemia (an oxygen deprived state). Subsequent release of the renal artery clamp enables reperfusion of the ischemic kidney. Ischemia-reperfusion of this sort is a classic model of renal tubular cell injury. It is the renal tubular cells that are the most susceptible to ischemic injury, as these cells normally live in a low oxygen environment. When the kidney is challenged by low oxygen tension, as is the case with renal artery clamping, it is the tubular cells that suffer the burden of injury. This is often referred to as acute tubular necrosis, or ATN. The initial tubular injury results in altered nephron architecture, obstruction, and reduced clearance. Importantly, ischemia reperfusion injury is not a form of primary glomerular cell injury, as is the case with the Thy 1 nephritis model. Similarly, the Thy 1 nephritis model does not directly involve the renal tubular cells, and this model is not characterized by obstruction and disturbed nephron architecture. Thus, Imai does not teach the treatment of acute kidney dysfunction nor does it teach a subject in need thereof.

Thus, Imai does not teach each and every limitation of claims 1, 2, 6-9, 49-50 and 60 and cannot anticipate them. Applicants respectfully request that this rejection be withdrawn.

1/ *See* Imai at page 792.
2/ *Id.* at left column.
3/ *Id.*

The Examiner has rejected claims 51 and 52 under 35 U.S.C. § 102(a) for being anticipated by Tabata. (*See* Final Office Action at page 6). Applicants have canceled claims 51 and 52, without prejudice or disclaimer, thereby rendering this rejection moot.

The Examiner has also rejected claims 51 and 52 under 35 U.S.C. § 102(a) for being anticipated by Caplan. (*See* Final Office Action at pages 6-7). Applicants have canceled claims 51 and 52, without prejudice or disclaimer, thereby rendering this rejection moot.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submits that the pending claims are in condition for allowance. Applicant respectfully requests prompt examination in the application. If there are any questions regarding this Submission, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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